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EXAMINER

FOLEY, SHANON A

ART UNIT

PAPER NUMBER

1648

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/937,862

Applicant(s)

OBERSTE ET AL.

Examiner

Shanon Foley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) 3-5 and 12-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2 and 6-11 is/are rejected.
- 7) ☒ Claim(s) 7 and 8 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> . | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I and SEQ ID NOs: 19 and 22 in Paper No. 9 is acknowledged.

Although applicant elected group I with traverse, applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, therefore, the election of group I has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's traversal for electing primers, SEQ ID NO: 19 and 22, is on the grounds that at least 10 primers should be examined according to MPEP § 803.04. Applicant further asserts that since claim 1 is generic to any primer, the specific primer pairs in subsequent claims should be based on a species election only. Applicant states that they are entitled to a reasonable number of the claimed sequences upon finding a generic claim patentable under the species election.

Applicant's arguments have been considered, but are found unpersuasive. While claim 1 is generic to primers used in the method of detecting the presence of an enterovirus, the special technical feature defining claim 1 lacks novelty in the prior art, as evidenced by claims 1 and 8 of Kilpatrick (WO 98/14611). Since the special technical feature of group I lacks novelty in the art, any subsequent group that does not share the special technical feature with group I lacks unity of invention. Subsequent groups II-IV do not share the same method steps and/or components defining the special technical feature of group I. Further, all of the instant oligonucleotides do not share the special technical feature with any group and each are structurally and functionally distinct.

The restriction requirement between the primer sequences is proper. MPEP § 803.04 discusses restriction between nucleotide sequences in nationally filed applications filed under 35 U.S.C. 111. This application is an internationally filed application filed under 35 U.S.C. 371 and is subject to the rules discussed under MPEP § 1850 (see the last paragraph under MPEP § 803.04, which references the appropriate section for internationally filed applications). Under Markush practice for international applications, the following criteria are required:

(A) the alternatives have a common property or activity and (B) a common core structure is present; or

(C) in cases where the core structure cannot be the unifying criteria, all alternatives must belong to the same recognized class of chemical compounds, that is, that the same result will be achieved when one member of the Markush group is substituted for another.

In the instant case, none of the oligonucleotides can hybridize to the same nucleic acid sequence or amplify the same product and they do not share a common core structure. Therefore, the primers do not meet the criteria for (A) and (B). Also, each pair oligonucleotides do not meet criteria (C) because each pair will amplify a different portion of a nucleic acid and different products will be generated. Therefore, the same result is not achieved when one of the primers within a pair is substituted for another or when different pairs are used. Since the instant oligonucleotides do not share the same or corresponding special technical feature under the specific criteria for Markush practice, the oligonucleotides lack unity of invention and are not considered alternative species to one another. Therefore, applicant's proposed species election would be improper.

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MPEP § 1850 also discusses the unity of invention with regard to nucleotide sequences in internationally filed applications. This section states:

“Thus, in international applications, for each group for which applicant has paid additional international search and/or preliminary examination fees, the USPTO has determined that up to four (4) such additional sequences per group is a reasonable number for examination.”

In the instant case, no such additional fee is applicable because this a national stage filing of an international application.

For these reasons, the requirement is still deemed proper and is therefore made FINAL.

Claims 3-5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected oligonucleotide primers and the corresponding sequence motifs the primers hybridize to, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

Claims 12-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

Claims 1, 2 and 6-11 encompass the elected SEQ ID NOs: 19 and 22 and the corresponding sequence motifs the primers hybridize to. Claims 1, 2 and 6-11 are under consideration.

Specification

The disclosure is objected to because of the following informalities:

The specification is objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific amino acid sequences comprising four or more amino acids and ten or more nucleic acids in the specification. Specific examples within the specification that do not comply with the sequence rules are found on page 35, lines 17 and 22 and page 36 line 6. Applicant is required to append a SEQ ID NO. to any unidentified sequence within the disclosure that is applicable to the rule. See 37 CFR § 1.821 (a)-(d) and MPEP § 2422.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6 and 9-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Kilpatrick (WO 98/14611, provided in IDS).

Claim 1 is drawn to a method of detecting the presence of an enterovirus in a clinical sample by obtaining a clinical sample from a subject, purifying the RNA within the sample, reverse transcribing the RNA to provide a cDNA and contacting at least a portion of the cDNA a composition that promotes amplification of a nucleic acid with an oligonucleotide that hybridizes to a highly conserved sequence of a sense strand and an oligonucleotide that hybridizes to a

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highly conserved sequence of an antisense strand so that amplification of a portion of the VP1 within the enterovirus genome results and an enterovirus amplicon is produced, if an enterovirus is present, and detecting the presence of the amplicon, which denotes the presence of an enterovirus in a sample. Claim 2 states that the highly conserved sequences occur within the VP1 gene. Claim 6 requires that at least one of the oligonucleotides hybridizes to a specific motif, identified by a SEQ ID NO. Claim 9 states that the amplification is accomplished by PCR. Claim 10 lists types of clinical samples and claim 11 lists conventional methods of detecting amplified products.

Kilpatrick anticipates a method of detecting the presence of enterovirus nucleic in a biological sample such as whole blood, serum, urine, saliva, cerebrospinal fluid and semen, see page 7, lines 31-33 and page 11, lines 4-8. This teaching anticipates the limitations recited in instant claim 10. Kilpatrick teaches that the first step is amplifying cDNA from isolated enterovirus RNA in a sample, see page 15, lines 22-28 and page 16, lines 21-25. Highly conserved PCR primers target sense and antisense strands of enterovirus nucleotide sequences encoding highly conserved amino acid regions, see page 15, lines 4-7, page 16, lines 3-5. The PCR primers of Kilpatrick are derived from VP1 and are used to amplify conserved sequence motifs, see page 22, lines 23-31, Table 1 on page 23, claims 1, 3, 4 and 8. This teaching anticipates claim 2. The amino acid sequence motif designated by SEQ ID NO: 2 in claim 4 of Kilpatrick corresponds to the sequence motif, SEQ ID NO: 86 (described on page 43, lines 13-14 of the instant disclosure) that instant SEQ ID NO: 22 binds to. Therefore, Kilpatrick anticipates using a primer in the method that specifically hybridizes to the motif given by SEQ ID NO: 86 in instant claim 6. Amplification of the nucleic acid is accomplished by PCR, see page 13, line 35

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to page 14, line 2 and page 15, lines 10-13. This teaching anticipates claim 9. The amplified products are detected conventionally by gel electrophoresis or labeled probes, see page 18, line 7 to page 19, line 29. This teaching anticipates claim 11 and the method steps for detecting an enterovirus in a sample anticipate claim 1.

Claims 1 and 9-11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kilpatrick et al. (Journal of Clinical Microbiology. February 1998; 36 (2): 352-357).

See the claim summary for claims 1 and 9-11 above.

Kilpatrick et al. clearly anticipate a method of determining the presence of poliovirus propagated in tissue culture cell lines by PCR-amplifying isolates using primers that bind to the conservative codons in the antisense strand of VP1 and primers that bind to the conservative codons on the sense strand of the capsid sequences, see the abstract and Figure 1 on page 354. The virus RNA is purified and reverse transcribed to yield cDNA that is amplified by PCR by the specific primers. Amplified products, which include at least a portion of VP1, are analyzed by gel electrophoresis, see "Viruses" on page 352, "PCR amplification and analysis" in the first column on page 353 and Figure 1. Therefore, Kilpatrick et al. clearly anticipate claims 1 and 9-11.

Claims 1, 2 and 9-11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kilpatrick et al. (Journal of Clinical Microbiology. 1996; 34 (12): 2990-2996).

See the claim summary for claims 1, 2 and 9-11 above.

Kilpatrick et al. clearly anticipate a method of determining the presence of poliovirus propagated in tissue culture cell lines by PCR-amplifying isolates using a pair of panpoliovirus primers that bind to the antisense and sense strands of conservative codons within the VP1 gene.

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The virus RNA is purified and reverse transcribed to yield cDNA that is amplified by PCR by the specific primers. Amplified products, which include at least a portion of VP1, are analyzed by gel electrophoresis, see the abstract, "Viruses" on page 2990, "Oligonucleotide synthesis" bridging pages 2990-2991, "PCR amplification and analysis" in the first column on page 2991, Figure 1 on page 2991, Figure 2 on page 2992 and Figure 3 on page 2993. Therefore, Kilpatrick et al. clearly anticipate claims 1, 2 and 9-11.

Allowable Subject Matter

Claims 7 and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 7 and 8 require that an oligonucleotide primer used to detect the presence of enterovirus in a sample comprises SEQ ID NO: 22 and that the other primer comprises SEQ ID NO: 19. While Kilpatrick et al. (WO 98/14611) teaches a primer, V3A, comprising SEQ ID NO: 22 (see the sequence alignment provided), the reference does not teach or suggest a primer comprising SEQ ID NO: 19 or using a primer comprising SEQ ID NO: 22 with a primer comprising SEQ ID NO: 19.

The prior art does not teach or suggest a primer comprising SEQ ID NO: 19 or using a primer comprising SEQ ID NO: 22 with a primer comprising SEQ ID NO: 19.


Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4426 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


Shanon Foley
June 26, 2003